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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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09/436,513 11/09/99 JONES

J 3290.007US1

EXAMINER

HM12/1004

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ART UNIT

PAPER NUMBER

1652

DATE MAILED:

10/04/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application N .

09/436,513

Applicant(s)

JONES ET AL

Examiner

Charles L. Patterson, Jr.

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 25 July 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13, 21-57, 59, 61 and 62 is/are pending in the application.
- 4a) Of the above claim(s) 21-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13, 51-57, 59, 61 and 62 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other:

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Claims 21-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1-11, 13, 51-57, 59 and 61-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In Figure 3 the recitation of "MOM" is not understood and in Figure 4 the recitation of "Bn" is not understood. Applicant states that "MOM" stands for "Methoxymethyloxy" and that this is described on page 18, line 30 and page 26, line 20. In the first case only the abbreviation "MOM" is recited without a definition" and in the second case "methoxymethyloxy" is recited without the abbreviation. Applicant further states that "Bn" is the abbreviation for "benzyl" and state that this is found on page 40, lines 10-24 and Scheme (Fig. 2) and Scheme 3 (Fig. 3). In this case the abbreviation is found in Figure 2 without the definition and is not found in Figure 3. Applicant should provide either a reference in the specification where these abbreviations are defined or else a reference in the prior art using these abbreviations where the definitions are given.

In Table 2, it was asked what "4", " $\pm 0.05$ ", " $\pm 180$ ", " $\pm 0.07$ ", " $\pm 540$ ", "..." $\pm 710$ ", " $\pm 407$ " mean in the second, fourth, sixth and eighth lines. Although applicants did not answer this question, upon further review it is concluded that these are the standard errors of the values above them. However, it is not understood why " $\pm$ " is after the values above in some cases

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and with the standard errors in others. Applicants have satisfactorily explained the first part of the previous question regarding the fifth and ninth columns.

Claims 1-11, 13, 51-57, 59 and 61-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Bacillus lentus subtilisin* N62C-a, N62C-d, N62C-e, N62C-f (R isomer only), N62C-h, N62C-i (R isomer only), S166C-d (S isomer only), S166C-h (S isomer only), S166C-I (S isomer only), L217C-a, L217C-b, L217C-d, L217C-e, L217C-f and L217C-i, does not reasonably provide enablement for the scope of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant mutations give an increase in activity for amidase and/or esterase above the standard error of the wild type while the other mutations do not (Table 1). The other mutations would not have a utility as they would have less activity than the wild type. Note, N62C-c, S166C-c and L217C-c and the modifications discussed in Example 2 are omitted from the list *supra* because they do not meet the requirement of claim 1 that the thiol side chain is chiral.

In Table A provided with the amendment as an explanation of the chemical names of the compounds, the structures are listed as "(R)-1a", "(S)-1a", etc. Figures 2 and 4 and Tables 1-3 use the notation "N62C-a", etc. It is presumed that "(R)-1a" is meant to be the (R) isomer of the "a" cysteine change at a given position, e.g. N62. The "1a" is not found except for the 3 structures in the upper right hand corner of Fig.3 and in several places in the specification such as page 30, lines 3 and 26, page 31, line 28, page 32, line 28, etc. This discrepancy is not understood.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11, 13, 51-57, 59 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berglund, et al. (A or C2), Davis, et al. (C3) or DeSantis, et al. (C4). The instant reference all teach the concept of altering a serine protease by changing some residue to cysteine and then altering the thiol side chain of the cysteine by chemical means. Widely varying results depending on the residue altered and the chemical change. See for example Tables 1 and 2 of Berglund, et al. (A), Table 1 of Berglund, et al. (C2) and Table 1 of DeSantis, et al. (C4). It would have been obvious to one of ordinary skill in the art to modify serine proteases as done in the instant references and assay them for activity, absent unexpected results. The motivation would have been to obtain different mutant enzymes that may have some use. Given the wide range of results obtained in the instant references it is not unexpected that a wide range of results were obtained in the instant application. Whether or not the chemical side chain alteration are chiral or not do not affect this rejection. Wide variations are obtained with both chiral and non-chiral changes.

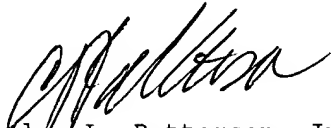
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose

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telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-7401 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Charles L. Patterson, Jr.  
Primary Examiner  
Art Unit 1652

Patterson  
October 3, 2001